EXHIBIT 17

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY JANUARY 2017, VOL. 38, NO. 1

ORIGINAL ARTICLE

Association of Airborne Microorganisms in the Operating Room With Implant Infections: A Randomized Controlled Trial

Rabih O. Darouiche, MD;[1] David M. Green, MD;[2] Melvyn A. Harrington, MD;[3] Bruce L. Ehni, MD;[4] Panagiotis Kougias, MD;[5] Carlos F. Bechara, MD;[6] Daniel P. O'Connor, PhD[7]

OBJECTIVE. To evaluate the association of airborne colony-forming units (CFU) at incision sites during implantation of prostheses with the incidence of either incisional or prosthesis-related surgical site infections.

DESIGN. Randomized, controlled trial.

SETTING. Primary, public institution.

PATIENTS. Three hundred patients undergoing total hip arthroplasty, instrumented spinal procedures, or vascular bypass graft implantation.

METHODS. Patients were randomly assigned in a 1:1 ratio to either the intervention group or the control group. A novel device (Air Barrier System), previously shown to reduce airborne CFU at incision sites, was utilized in the intervention group. Procedures assigned to the control group were performed without the device, under routine operating room atmospheric conditions. Patients were followed up for 12 months to determine whether airborne CFU levels at the incision sites predicted the incidence of incisional or prosthesis-related infection.

RESULTS. Data were available for 294 patients, 148 in the intervention group and 146 in the control group. CFU density at the incision site was significantly lower in the intervention group than in the control group ($P < .001$). The density of airborne CFU at the incision site during the procedures was significantly related to the incidence of implant infection ($P = .021$). Airborne CFU densities were 4 times greater in procedures with implant infection versus no implant infection. All 4 of the observed prosthesis infections occurred in the control group.

CONCLUSION. Reduction of airborne CFU specifically at the incision site during operations may be an effective strategy to reduce prosthesis-related infections. Trial Registration: clinicaltrials.gov Identifier: NCT01610271

Infect Control Hosp Epidemiol 2017;38:3–10

Surgical site infections (SSI) following implantation of prostheses are a growing problem. The total number of implant infections that occur after total hip and knee arthroplasty in the United States is projected to increase from 22,000 in 2009 to 65,000 in 2020 and with healthcare costs exceeding $1 billion per year by 2020.[1]

Microorganisms responsible for prosthesis infections are commonly transported in surgical theater air,[2–4] whereby they may enter incision sites during surgical procedures and cause SSI.[5–7] The primary source of these airborne microorganisms is the people in the operating room, such that the number of people, door openings, and room traffic all increase the quantity of airborne colony-forming units (CFU).[8–10]

Current methods for reducing airborne CFU in the operating room during prosthesis implantation include the use of surgical gowning with exhaust hoods, laminar flow air systems, ultraviolet light, and limiting room traffic.[11,12] These methods largely attempt to alter the environment of the entire operating room in a manner that is remote from the surgical site. A more efficient tactic may be to control the airborne environment immediately surrounding the incision site, where the presence of CFU has a greater likelihood of depositing onto the prosthesis.[12–14] However, to our knowledge, no literature has indicated whether the density of airborne CFU measured at incision sites is related to increased incidence of SSI. Thus, the purpose of this study was to evaluate whether airborne CFU density at the incision site during operations is related to

Affiliations: 1. Departments of Medicine, Surgery, and Physical Medicine and Rehabilitation, Michael E. DeBakey Veterans Affairs Medical Center (VAMC), and Infectious Disease Service, Baylor College of Medicine, Houston, Texas; 2. Section of Orthopedic Surgery, Michael E. DeBakey VAMC, Houston, Texas; 3. Baylor College of Medicine Medical Center, Houston, Texas; 4. Section of Neurosurgery, Michael E. DeBakey VAMC, Houston, Texas; 5. Section of Vascular Surgery, Michael E. DeBakey VAMC, Houston, Texas; 6. Houston Methodist Cardiovascular Surgery Associates, Houston, Texas; 7. University of Houston, Houston, Texas.

Received July 18, 2016; accepted September 15, 2016; electronically published October 26, 2016

 0899-823X/2017/3801-0002. DOI: 10.1017/ice.2016.240

the incidence of incisional or implant infections after placing the prostheses.

METHODS

Design and Patients

This prospective, randomized clinical trial was conducted from January 19, 2012, through April 2, 2015, at the Michael E. DeBakey Veterans Affairs Medical Center using a parallel groups design. Inclusion criteria were patients at least 18 years old undergoing primary or revision total hip arthroplasty, posterior lumbar fusion or cervical laminectomy with instrumentation, or lower extremity vascular bypass with prosthetic or bovine graft. Exclusion criteria included history of prosthesis infection or presence of an active infection. Patients were evaluated for eligibility by a research associate who was not involved in their care. The institutional review board of Baylor College of Medicine approved this study, and all patients provided signed informed consent.

Patients were randomly assigned in a 1:1 ratio to either the intervention or control group using a block randomization scheme with mixed block sizes (randomly ranging from 2 to 8) to attain balanced group sizes for strata defined both by procedure type and by primary or revision implantation. Randomization lists were created using NQuery Advisor, version 7.0 (Statistical Solutions), before recruitment began by a biostatistician not involved in the care or assessment of patients. Group assignment was made after consent by the research associate. A sample size of 150 per group provided a power of 80% to detect a statistically significant ($\alpha \leq .05$) 3% difference in SSI rate on the basis of a historical infection rate of 6% in the facility where operations were performed. The SSI difference between groups was the planned comparison that had the lowest power, so a sample size designed to obtain adequate power for this test would have adequate power for all other planned comparisons, including the primary hypothesis of an association between CFU density and SSI.

Interventions

All implants, perioperative care, and surgical procedures were determined by the surgeons' and facility's routine practices and were unaffected by this investigation. Total hip arthroplasty procedures used the posterolateral approach, spinal procedures used the posterior approach, and vascular procedures used the anterior approach. All procedures were performed in operating rooms designed with conventional air handling systems compliant with the Centers for Disease Control and Prevention guidelines.[15] Skin antiseptic varied by procedure type but was the same for both study groups: total hip arthroplasty used chlorhexidine gluconate and isopropyl alcohol solution (ChloraPrep; Becton, Dickinson); spinal procedures used iodine povacrylex and isopropyl alcohol solution (DuraPrep; 3M); vascular bypass used betadine (Purdue Products) in year 1 and ChloraPrep in years 2 and 3. All 294 patients received cefazolin or vancomycin for antibiotic prophylaxis, either as the only antibiotic (146 [49.7%]), both together (19 [6.5%]), or combined with another antibiotic (129 [43.9%]), intraoperatively and for 1 to 4 days postoperatively with weight-based dosing per the surgeons' routine practices. Per routine care in the study facility, silver-impregnated dressings were used after all hip procedures whereas plain gauze dressings were used after all spine and vascular cases. Surgical staff wore hoods in all hip procedures but not in spinal and vascular cases. The operating surgeon and surgical team could not be masked to the intervention but were involved in neither the assignment to groups nor the evaluation of SSI.

Intervention group. In the intervention group, all operations were performed with protection against airborne CFU and particulate at the incision site using the Air Barrier System device (ABS; Nimbic Systems). The ABS, which is cleared for sale by the US Food and Drug Administration, creates a positive pressure, nonturbulent clean air envelope that shields open surgical wounds from airborne CFU and particulate during an operation. It passes ambient air through a filter that removes 99.997% of particulate sized 0.3 μm or larger in diameter and issues it through a hose to a nozzle attached on top of the incision drape within a few inches of the incision (Figure 1). The clean air passes over the surgical field and effectively shields an area of 16 cm wide × 53 cm long.

Airborne particulate and CFU were collected simultaneously through two 244-cm sterile tubes affixed at the incision site (Figure 2). A particle counter (Lasair 310; Particle Measuring Systems) drew air through 1 tube at 28.3 L/min and enumerated the particulate in the airstream. Air was drawn at 28.3 L/min through the second tube into an Andersen-style bioaerosol collection device (EMS E6; Environmental Monitoring Systems) and onto agar plates (tryptic soy agar, 5% sheep's blood) that were exchanged every 10 minutes throughout the procedures. Control plates were exposed momentarily to ambient air as a negative control for handling and processing contamination.

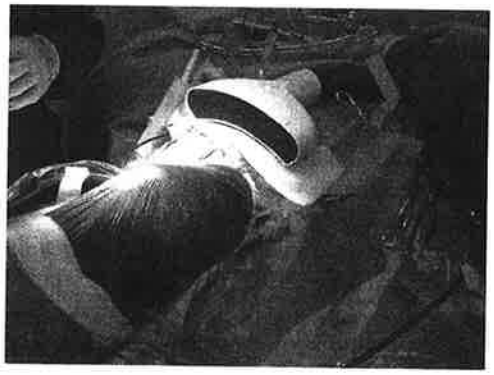

FIGURE 1. The Air Barrier System passes ambient air through a filter that removes 99.997% of particulate sized 0.3 μm or larger in diameter and issues it through a hose to a nozzle attached on top of the incision drape within a few inches of the incision.

The plates were incubated at 35°C for 36 hours by an independent laboratory (Hygeia Labs), and viable organisms were identified and reported as CFU per cubic meter.

Control group. The control group operations were conducted according to usual practice without the ABS. Airborne particulate and CFU densities were captured at 10-minute intervals exactly as described in the intervention group.

Data Collection

Patient characteristics recorded from the medical record included gender, ethnicity, age, and body mass index (calculated as weight in kilograms divided by height in meters squared). Comorbid indicators for increased SSI risk included American Society of Anesthesiologists score, medical history (cardiopulmonary disease, neurological condition, cancer, and diabetes mellitus), currently smoking, malnutrition, and history of SSI in previous year.

Operation- and procedure-related data included surgeon, operating room, antibiotic prophylaxis, number of people in the operating room at the beginning of each 10-minute interval, operative time, revision or primary procedure, and procedure type. During the operations, data were collected by a research technician who was responsible for counting the number of people and exposing and replacing the agar plates every 10 minutes.

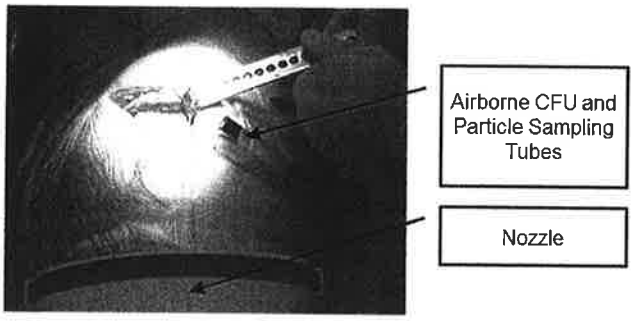

FIGURE 2. Airborne particulate and colony-forming units (CFU) were collected simultaneously through two 244-cm sterile tubes affixed at the incision site.

Particulate densities were reported as particles per cubic meter at several size thresholds (0.3 μm, 0.5 μm, 1 μm, 5 μm, and ≥10 μm). Because operative time ranged widely (64 to 523 minutes), only particulate and CFU densities during the first 100 minutes of each case were analyzed. Counts obtained during the first 100 minutes did not differ significantly from counts over the full duration of each case ($P \geq .88$).

While residing in the hospital, postoperative patients were followed up daily by a research nurse who did not get involved in patients' care and who daily reviewed the medical records for documentation of the presence of symptoms and signs of SSI that had been established by a physician. The research nurse followed up with the patients by telephone at 1 month after the surgical procedure and then every month for 12 months so as to document the presence or absence of SSI. Diagnosis of SSI was made by a physician who was masked to the patients' group assignment and not involved in the patients' care by evaluating medical records using the Centers for Disease Control and Prevention criteria,[16] which categorize SSI into superficial incisional, deep incisional, and organ/space/implant levels. Superficial and deep incisional infections were defined and reported as "incisional" infections, whereas organ/space/implant level infections were defined and reported as "implant" infections.

Statistical Analyses

All analyses were intention to treat, which included 294 (98%) of the 300 randomized participants. Six randomized patients (2 intervention, 4 control) were excluded from analysis because they did not receive an implant and thus were not at risk for implant infection (Figure 3). One of the intervention

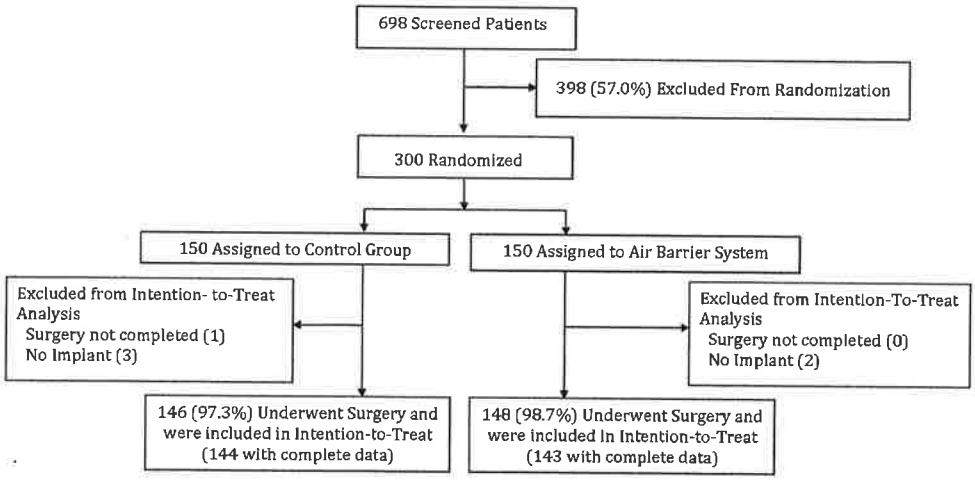

FIGURE 3. Flow chart of randomized controlled trial examining association of airborne microorganisms in the operating room with implant infections.

patients was missing CFU and particulate data and was excluded from the analyses requiring those data. An additional 6 participants (4 intervention, 2 control) were missing particulate data only and were excluded from the analyses requiring the particulate data. These participants were included in all other analyses, including incidence of infection.

The relation of SSI to CFU density was tested using penalized maximum likelihood logistic regression.[17,18] The associations of group and covariates with particulate and CFU density were evaluated using negative binomial regression and zero-inflated negative binomial regression, respectively, with robust (Huber-White) standard errors.[19] Group differences for incidence of infection were tested using Fisher exact tests. All data were analyzed using Stata, version 13 (StataCorp).

RESULTS

Two participants in the intervention group and 2 participants in the control group died before the 12-month follow up for reasons unrelated to their operations. These 4 participants were included in all analyses; none had been diagnosed with SSI at the time of death. All other participants (290 [98.6%] of 294) completed 1-year follow-up.

Patient and Operation Characteristics

The intervention and control groups did not differ significantly with respect to patient or operation characteristics ($P>.05$, Table 1). The operations were performed by 9 different surgeons in 9 different operating rooms, distributed equally across the study groups. Most of the patients were men, consistent with the Veterans Affairs population, and older than 55 years. The intervention group had significantly more smokers (73.7%) than the control group (59.6%, $P=.013$). There were no other significant group differences for other SSI risk factors and comorbidities ($P>.30$, Appendix Table 1).

None of the patient characteristics were significantly associated with the particulate density, CFU density, or infection ($P>.10$) (Appendix Table 2). The number of people in the operating room was positively related to CFU density in both the intervention ($P=.006$) and control ($P=.019$) groups.

CFU and Particulate Densities

Across all procedure types, the intervention group using ABS had significantly ($P<.001$) lower particulate and CFU densities compared with the control group. In the intervention group, 68.1% of the 10-min surgical intervals collected during the study had 0 CFU/m^3, compared with 46.1% in the control group ($P<.001$). Within each procedure type, the intervention group had lower median particulate density compared with the control group (Table 2).

CFU and Particulate Densities and Infection

CFU density at incision sites was significantly related to incidence of implant infection ($P=.021$), but not of incisional infection ($P=.687$). Every 10 CFU/m^3 increase in median CFU density approximately doubled the probability of implant infection (Figure 4). CFU density was positively related to total particulate density ($P<.001$) in the control group, indicating that airborne particle counts may be used as a proxy for ambient CFU density. No association between particle density and CFU could be demonstrated in the intervention group because 68.1% of the 10-minute intervals had 0 CFU and provided no significant variation in CFU levels (Figure 5).

TABLE 1. Descriptive Statistics by Group, Procedure Type, and Primary or Revision Operation

		Total hip arthroplasty		Spinal procedure		Vascular bypass	
	Variable	Primary	Revision	Primary	Revision	Primary	Revision
Intervention	Sample size	64	9	62	4	7	2
	Male sex, %	90.6%	88.9%	98.4%	100%	100%	100%
	White race, %	59.4%	66.7%	61.3%	25%	85.7%	0%
	Age, y	61.3 ± 10.8	67.7 ± 10.3	60.1 ± 8.9	55.3 ± 12.1	62.6 ± 4.8	59.0 ± 7.1
	BMI	28.8 ± 4.7	31.3 ± 5.9	29.1 ± 5.4	30.6 ± 6.6	24.6 ± 5.5	29.9 ± 9.6
	People in OR, no.	9.5 ± 1.1	10.5 ± 0.8	7.3 ± 1.1	8.0 ± 1.3	8.1 ± 1.0	8.0 ± 1.2
	Operative time, min	139.6 ± 38.5	204.7 ± 77.2	196.9 ± 76.1	260.8 ± 68.8	268.0 ± 98.6	406.0 ± 165.5
Control	Sample size	64	9	62	4	7	0
	Male sex, %	93.8%	100%	93.6%	100%	100%	n/a
	White race, %	62.5%	33.3%	59.7%	50%	57.1%	n/a
	Age, y	63.6 ± 11.4	60.3 ± 9.4	58.7 ± 10.2	68.3 ± 8.8	60.6 ± 5.2	n/a
	BMI	29.0 ± 4.4	30.0 ± 5.1	29.9 ± 4.5	28.5 ± 5.5	29.4 ± 4.7	n/a
	People in OR, no.	9.4 ± 1.3	9.7 ± 1.2	7.4 ± 1.1	8.6 ± 1.3	7.4 ± 1.0	n/a
	Operative time, min	142.6 ± 38.3	201.6 ± 78.6	210.5 ± 83.4	276.3 ± 106.7	260.7 ± 119.1	n/a

NOTE. Data are mean ± SD unless otherwise indicated. BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); n/a, not applicable; OR, operating room.

TABLE 2. Densities of Total Particulate and Colony-Forming Units (CFU) per Cubic Meter by Study Group and Procedure Type

Total hip arthroplasty							
	Control (n = 73)			Intervention (n = 69)			
Variable	Median	25th percentile	75th percentile	Median	25th percentile	75th percentile	*P*
Total particulate	196,185	106,160	360,825	62,677	20,764	221,240	<.001
CFU	4	2	6	0	0	3	<.001
Spinal procedure							
	Control (n = 66)			Intervention (n = 65)			
Variable	Median	25th percentile	75th percentile	Median	25th percentile	75th percentile	*P*
Total particulate	198,227	102,318	425,227	125,780	45,652	260,594	.014
CFU	2	0	4	0	0	0	<.001
Vascular bypass							
	Control (n = 7)			Intervention (n = 9)			
Variable	Median	25th percentile	75th percentile	Median	25th percentile	75th percentile	*P*
Total particulate	121,850	86,762	143,293	10,482	1,093	13,371	.030
CFU	0	0	2	0	0	0	.392

NOTE. The subsample sizes (n) are the number of patients with particulate data in each subgroup; 2 patients in the control group (both hip arthroplasty cases) and 4 patients in the intervention group (1 spinal and 3 hip arthroplasty cases) were missing particulate data. One patient in the intervention group (hip arthroplasty) was missing both particulate and CFU data. *P* values are for comparisons of median values between control and intervention groups at each respective particulate size or CFU density.

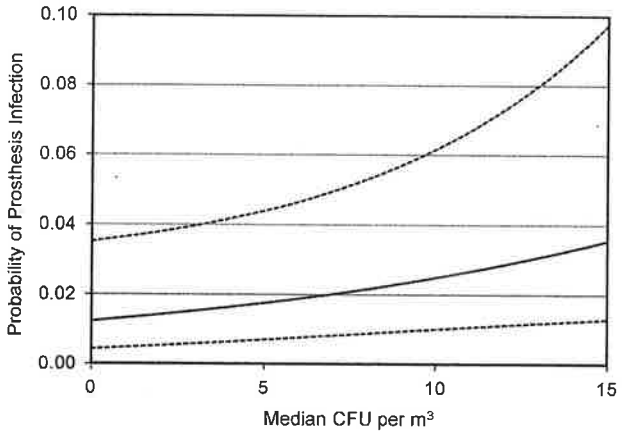

FIGURE 4. Graph of density of colony-forming units (CFU) at incision sites and probability of implant infection (*P* = .021). Dashed lines represent 95% CIs.

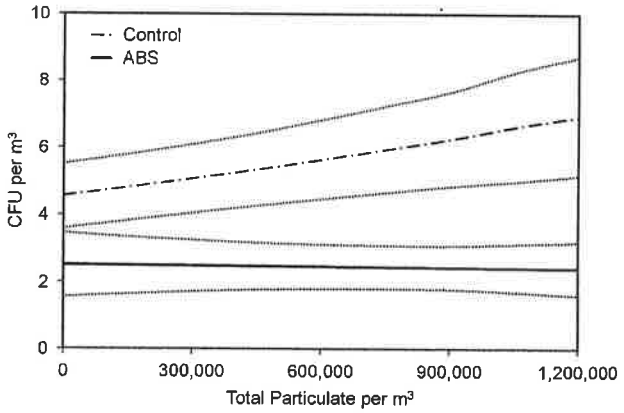

FIGURE 5. Graph of particulate density and colony-forming units (CFU). Dotted lines represent 95% CIs. ABS, Air Barrier System.

No patients in the intervention group (0% [95% CI, 0%–2.5%]) had implant infections, whereas 4 patients in the control group (2.7% [0.7%–7.0%]) had implant infections at 8, 11, 27, and 58 days after operation, respectively. Pathogens included methicillin-resistant *Staphylococcus aureus* in 1 case, methicillin-sensitive *S. aureus* in 2 cases, and multiple organisms (*Proteus mirabilis*, *Providencia stuartii*, and *Enterococcus faecalis*) in 1 case. Species identification for the airborne CFU samples was too complex and was beyond the scope and purpose of the study.

Of the 148 participants in the intervention group, 4 (2.7% [95% CI, 0.7%–6.9%]) had incisional infections at 3, 8, 32, and 32 days after operation (methicillin-resistant *S. aureus* in 1 case, methicillin-sensitive *S. aureus* in 1 case, *Pseudomonas* in 1 case,

and no cultures in 1 case). Three participants in the control group (2.0% [0.4%–6.0%]) had incisional infections at 4, 14, and 16 days after operation (methicillin-resistant *S. aureus* in 1 case, no growth in 1 case, and no cultures in 1 case).

The incidence of incisional infection differed by procedure type ($P=.025$): total hip arthroplasty (0.7%, 1/146), spinal procedure (3.0%, 4/132), and vascular bypass (12.5%, 2/16). In contrast, procedure type was not significantly associated with incidence of implant infection ($P=.700$): total hip arthroplasty 2.0% (3/146), spinal procedure 0.8% (1/132), and vascular bypass 0% (0/16).

DISCUSSION

To our knowledge, this is the first randomized, controlled study of the relationship between the levels of intraoperative airborne CFU adjacent to incision sites during prosthesis implantation and incidence of SSI. Analyses included CFU counts collected during 2,822 10-minute intervals, and a total of 11,039 CFU were cultured from the air during 470 hours of operative time. Our findings demonstrate that these microorganisms are significant sources of implant infections, and that reducing them within the surgical field also reduced the incidence of implant infection.

While the Centers for Disease Control and Prevention acknowledges the importance of minimizing the presence of airborne CFU in operating rooms, it provides no guidelines for acceptable limits during surgery.[15] Our study confirms previous reports indicating that the levels of airborne CFU in the operating room are dependent on the number of people present.[3,8,20] However, efforts to limit room traffic may not be effective in practice, as described in studies wherein operating room doors were opened 50–60 times during orthopedic joint replacement.[3,21]

A prior study demonstrated that the ABS reduced CFU levels adjacent to incision sites,[20] and we employed the ABS to create a significant difference in CFU levels between study groups so that our hypothesis could be tested. In our study, there were 4 implant infections of 146 procedures in the control group and no implant infections of 148 procedures in the intervention group. At an estimated additional expense of $40,000 per infection in the control group, the 4 infections cost $160,000 to treat whereas the cost of using the ABS in those procedures would be approximately $35,000. In this scenario, prevention of a single infection would have been cost-saving. The positioning of the ABS was generally acceptable to the surgeons and did not present any technical challenges to performing the procedures.

Our study indicates that airborne CFU entering incisions during operations is a likely source of contamination leading to implant infections. Incisional infections, however, may result from a broader set of intraoperative and postsurgical factors, as suggested by studies reporting that skin preparation methods were associated with incisional but not organ/space SSI,[22,23] which would explain why we found no difference in rates of incisional infection. These findings indicate that appropriate control of the operating room atmosphere may complement other techniques, such as skin antisepsis, to provide a more comprehensive infection prevention strategy while implanting prostheses.

Our study design provides advantages over previous research regarding airborne contamination in the operating room. Contradictory findings in prior reports may be attributed to many factors, including nonrandomized comparisons of important risk factors and often lack of appropriate controls.[24–26] We used a stratified block random assignment that resulted in balance between the groups on relevant measured and unmeasured patient and surgical factors such that other factors could not have caused any observed differences in infection rates. The diagnosis of infection in our study was made by a physician who was masked to group assignment to minimize bias. This study, however, had some limitations. The presence of the ABS in the operating room may have affected the behavior of operating surgeons. However, the operating surgeons did not subsequently assess the presence, or lack thereof, of the occurrence of SSI. Also, the observed SSI incidence in the control group was lower than the historical average, which limited the power to detect statistically significant differences in SSI between groups. A larger randomized controlled, multicenter clinical trial would have a greater power in assessing the clinical efficacy of the ABS in reducing prosthesis-related infections.

In conclusion, our results indicate that CFU contamination of air at the incision site is a risk factor for implant but not incisional infections. CFU contamination is related to the particulate density in the air at the incision site, and both CFU and particulate density are a function of the number of people in the operating room. Limiting airborne CFU contamination at the incision site can be expected to lower implant infection risk.

ACKNOWLEDGMENTS

Financial support. National Institute of General Medical Sciences of the National Institutes of Health (award R44GM095005). Nimbic Systems provided assistance with particle count and CFU data acquisition.

Potential conflicts of interest. R.O.D. reports that he received grants from the National Institutes of Health during the conduct of the study; and that he was the director of the annual educational meetings of Multidisciplinary Alliance Against Device-Related Infection, which received education funds from Nimbic Systems, the manufacturer of the ABS. D.P.O. reports that he received consultant fees paid for statistical analyses from the National Institute of General Medical Sciences of the National Institutes of Health (award R44GM095005). All other authors report no conflicts of interest relevant to this article.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Address correspondence to Rabih O. Darouiche, MD, Departments of Medicine, Surgery, and Physical Medicine and Rehabilitation, Michael E. DeBakey VAMC, Bldg 100, Rm 4B-370, 2002 Holcombe Blvd, Houston, TX 77030 (rdarouiche@aol.com).

REFERENCES

1. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. *J Arthroplasty* 2012;27:61–65.
2. Edmiston CE Jr, Sinski S, Seabrook GR, Simons D, Goheen MP. Airborne particulates in the OR environment. *AORN J* 1999;69:1169–1179.
3. Stocks GW, Self SD, Thompson B, Adame XA, O'Connor DP. Predicting bacterial populations based on airborne particulates: a study performed in nonlaminar flow operating rooms during joint arthroplasty surgery. *Am J Infect Control* 2010;38:199–204.
4. Wan GH, Chung FF, Tang CS. Long-term surveillance of air quality in medical center operating rooms. *Am J Infect Control* 2011;39:302–308.
5. Hamilton H, Jamieson J. Deep infection in total hip arthroplasty. *Can J Surg* 2008;51:111–117.
6. Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Airborne contamination of wounds in joint replacement operations: the relationship to sepsis rates. *J Hosp Infect* 1983;4:111–131.
7. Ritter MA. Operating room environment. *Clin Orthop Relat Res* 1999;369:103–109.
8. Andersson AE, Bergh I, Karlsson J, Eriksson BI, Nilsson K. Traffic flow in the operating room: an explorative and descriptive study on air quality during orthopedic trauma implant surgery. *Am J Infect Control* 2012;40:750–755.
9. Edmiston CE Jr., Seabrook GR, Cambria RA, et al. Molecular epidemiology of microbial contamination in the operating room environment: is there a risk for infection? *Surgery* 2005;138: 573–579.
10. Smith EB, Raphael IJ, Maltenfort MG, Honsawek S, Dolan K, Younkins EA. The effect of laminar air flow and door openings on operating room contamination. *J Arthroplasty* 2013;28:1482–1485.
11. Evans RP. Current concepts for clean air and total joint arthroplasty: laminar airflow and ultraviolet radiation: a systematic review. *Clin Orthop Relat Res* 2011;469:945–953.
12. Knobben BA, van Horn JR, van der Mei HC, Busscher HJ. Evaluation of measures to decrease intra-operative bacterial contamination in orthopaedic implant surgery. *J Hosp Infect* 2006;62:174–180.
13. Burke JF. Identification of the sources of staphylococci contaminating the surgical wound during operation. *Ann Surg* 1963;158:898–904.
14. Duhaime AC, Bonner K, McGowan KL, Schut L, Sutton LN, Plotkin S. Distribution of bacteria in the operating room environment and its relation to ventricular shunt infections: a prospective study. *Childs Nerv Syst* 1991;7:211–214.
15. Sehulster L, Chinn RY. Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep* 2003;52:1–42.
16. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1999;20:250–278.
17. Firth D. Bias reduction of maximum likelihood estimates. *Biometrika* 1993;80:27–38.
18. Heinze G, Schemper M. A solution to the problem of separation in logistic regression. *Stat Med* 2002;21:2409–2419.
19. Long JS. *Regression Models for Categorical and Limited Dependent Variables*. Thousand Oaks, CA: Sage; 1997:242–247.
20. Stocks GW, O'Connor DP, Self SD, Marcek GA, Thompson BL. Directed air flow to reduce airborne particulate and bacterial contamination in the surgical field during total hip arthroplasty. *J Arthroplasty* 2011;26:771–776.
21. Panahi P, Stroh M, Casper DS, Parvizi J, Austin MS. Operating room traffic is a major concern during total joint arthroplasty. *Clin Orthop Relat Res* 2012;470:2690–2694.
22. Darouiche RO, Wall MJ Jr, Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med* 2010;362:18–26.
23. Morrison TN, Chen AF, Taneja M, Kucukdurmaz F, Rothman RH, Parvizi J. Single vs repeat surgical skin preparations for reducing surgical site infection after total joint arthroplasty: a prospective, randomized, double-blinded study. *J Arthroplasty* 2016;31:1289–1294.
24. Andersson AE, Petzold M, Bergh I, Karlsson J, Eriksson BI, Nilsson K. Comparison between mixed and laminar airflow systems in operating rooms and the influence of human factors: experiences from a Swedish orthopedic center. *Am J Infect Control* 2014;42:665–669.
25. Ayliffe GA. Role of the environment of the operating suite in surgical wound infection. *Rev Infect Dis* 1991;13:S800–S804.
26. Miner AL, Losina E, Katz JN, Fossel AH, Platt R. Deep infection after total knee replacement: impact of laminar airflow systems and body exhaust suits in the modern operating room. *Infect Control Hosp Epidemiol* 2007;28:222–226.